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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,980	09/30/2003	Yaron Iian	Enz-64 (CIP)	9089

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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
03/24/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,980	IIAN ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-118, 120-123, 125, 126, 129-151, 154-169, 171-177, 183-185, 187, 189-191, 197, 198, 200-202* is/are pending in the application.

4a) Of the above claim(s) *2-5,7-10,12-42,46,53,55-58,61-74, 77-96,98-108,110-118,121-123,129-150,154-156, 158-160,171-177,183, 185,187,189, 190, 197, 198, 200-202* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,11,43-45,47-52,54,59,60,75,76,97,109,120,125,126,151,157,161-169,184 and 191* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication filed 1/3/2011.

Any rejection(s) and/or objection(s) not reiterated herein have been withdrawn.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are under current examination.

Claim Rejections - 35 USC § 112-NECESSITATED BY AMENDMENTS

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 169 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 169 recites the limitation "monosaccharide ceramide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is a new matter rejection.

Applicant amended the claims so that they are directed to (in part) the administration of an intermediary metabolite which is a beta-glycosylceramide. Note that a search for the terms "beta" and/or "glycosylceramide" reveals the "beta-glycosylceramide" was not disclosed in the instant specification as filed. Applicant alleges that support for a beta-glycosylceramide is found in the specification in Figure 1. Para. [0021] of the specification provides the following: "Figure 1 shows the chemical structure of Glucocerebroside." Figure 1 provides a specific compound, glucocerebroside, in contrast to the broader scope of a glycosylceramide. Separately, Figure 1 and its figure legend do not reveal a molecule in its beta configuration. Applicant is invited to specifically point to any support for a "beta-glycosylceramide". Note that Adar and Ilan (*J. of Immunotoxicology*, 2008) state that alpha-glycosylceramides have not been detected in mammals "thus far", although such molecules in their beta configuration have; see p. 215, col. 1. Thus, it has yet to be established that all glycosylceramides are only found in their beta configurations. Because the instant specification fails to disclose whether the molecules are alpha- or beta-anomeric structures and there is a lack of conclusiveness in the art, the use of the term "beta-glycosylceramide" is considered an unacknowledged limitation at the time of filing and is considered as new matter in the claims.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 126, 151, 157, 161-168, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Note that claim 125 is removed from this rejection following amendments.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolite is a *beta-glycosylceramide*, wherein the pathogenesis of the disease is derived from an inflammatory immune response (see claim 1 as a representative).

The following quotation from section 2163 of the MPEP is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed or through disclosure of a functional characteristic of the claimed

genus coupled with a known or disclosed non-functional characteristic (structure) that correlates to the function.

Structurally, the claims are broad with respect to a genus of mammalian metabolic intermediate comprising a beta-glycosylceramide. Note that while a specific definition for "a beta-glycosylceramide" is not provided by the specification, Adar and Ilan (*Journal of Immunotoxicology*, 2008) define a beta-glycosylceramide as the following: a naturally occurring glycolipid that is a metabolic intermediate in glycol-sphingolipid anabolic and catabolic pathways. Its synthesis from ceramide is catalyzed by glucosylceramide synthase…"; see p. 215, col. 1. Note that "glyco-" can refer to any sugar or monosaccharide.

Para. [008]-[009] of the instant specification, for example, provide the written support for a glucosylceramide or a galactosylceramide but not for all possible sugars:

> [0008] An intermediary metabolite or a T cell receptor ligand is used in the present invention for the treatment of disease. The intermediary metabolite or the T cell receptor ligand may comprise a lipid or conjugated biomolecule. The conjugated biomolecule may in turn comprise a glycolipid, lipoprotein, apolipoprotein, or glycoprotein other than antibodies, cytokines, or hormones. *A glycolipid may comprise a monosaccharide ceramide. A monosaccharide ceramide may comprise a glucosylceramide or galactosylceramide*.

[0009] Glucosylceramide is a naturally occurring glycolipid consisting of ceramide, to which glucose is attached. A ceramide, which is a sphingosine and a fatty acid, is the structural unit common to all sphingolipids. Sphingonlinpids have a variety of cellular functions. These include membrane structural roles and cell signaling participation. (Sullard et al., 2000 Journal of Mass Spectrometry 35: 347-353.) Glucosylceramide is made by the enzyme glucosylceramide synthase which attaches the two molecules together. (see FIG. 1 and FIG. 2). *An example of a glucosylceramide includes glucocerebroside, or a glucocerebroside analogue or derivative.*

According to the prior art, Sweeley (Pure & Appl. Chem., 1989) states that there are more than 200 compounds in the class of glycosphingolipids that have been isolated and chemically characterized (abstract). Sweeley also cites the following: "Simple arithmetic calculations indicate the enormous diversity of structures that are theoretically possible with a few different sugar constituents, disregarding the heterogeneity of the ceramide moiety. For example, there could be about 500 million different glycosphingolipids, containing a core of 5 sugar residues (Glc, Gal, GlcNAc and alNAc combinations) in the pyranose ring form and one or two Fuc or NeuAc residues" (p. 1308, para. 2). Also, see this reference for the diversity in ceramide structures on p. 1307-1308 and in Tables 1 and 2. A more recent review describes the glycosphingolipids as having a huge heterogeneity of structure comprising more than 60 different sphingoid bases and more than 300 different oligosaccharide chains that have

been described at the time of the publication (Degroote et al., Sem in Cell & Dev Bio, 2004).

While the prior art teach such a diversity of structures for an intermediate metabolite, note that *functionally* the claims are specific. For example, claim 6 requires that the result of the administration of an intermediary metabolite comprises changes in cytokine response, claim 44 requires the result is a decrease in the number or function of regulatory, immune-regulatory or NKT cells and claim 45 requires that the result is an increase in the number or function of regulatory, immune-regulatory or NKT cells.

The instant specification provides no structure to function correlations for the specific claimed functional limitations and merely describes the *modulatory* effects following the administration of a *single* compound, glucocerebroside. Based on the instant specification, it is not clear what the required structural features of a beta-glycosylceramide are so that administration of such would lead to a change in NKT cells and other responses as claimed. Thus, the instant specification fails to describe the genus of mammalian intermediary metabolites in a reasonable manner so that one of ordinary skill in the art can readily envision the claimed genus as well as establish any structure to function correlation of the genus of metabolites necessary in order to perform the specific functions as claimed.

In view of the broad scope of the claims for a glycosylceramide, which may comprise any sugar constituent, as evidences by the prior art and the lack of structure to function correlations for an adequate number of species, the claims are rejected for lacking adequate written description in the instant specification.

Response to Arguments

Applicant's arguments filed 1/3/2011 have been fully considered but they are not persuasive. Applicant argues that the claims as amended are directed to treatment with a beta-glycosylceramide, “which is known as a structurally similar class of compounds that includes the glucocerebroside utilized in the Examples”. Applicant further alleges that beta-glycosylceramides are “rather a limited group of structurally similar compounds known to have generally similar activities"; see p. 37 of Remarks.

This is not persuasive. As noted above, Sweeley teaches an enormous diversity of structures possible with a few different sugar constituents as well as the heterogeneity of the ceramide moiety; see discussion above. Separately, Applicant has not provided any evidence to support this diverse group of structures has generally similar activities, particularly in the treatment of a disease in which the pathogenesis of the disease is derived from an inflammatory immune response. This is merely provided as an allegation. Of note, it is expected that compounds of different structures would be correlated to different functional properties. Because the claim is still broad in view of the claimed structures and the instant specification fails to provide any correlation between structure and function (e.g. a specific monosaccharide is required to bind to a specific receptor of a specific cell population etc), this rejection is maintained for reasons of record.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulating immune

responses via administration of glucocerebroside, does not reasonably provide enablement for the treatment of any and all diseases derived from an inflammatory immune response in a mammalian subject comprising administering any and all beta-glycosylceramide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/ use the invention commensurate in scope with these claims.

Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolite is a beta-glycosylceramide, wherein the pathogenesis of the disease is derived from an inflammatory immune response (see claim 1).

Scope of the invention. The claims are extremely broad with respect to both a beta-glycosylceramide and a disease that is derived from an inflammatory immune response. Also, see claim 157 which is drawn to a list of different diseases as well as "any other immune-related or immune-mediated disorder or disease".

State of the prior art. As noted above, the prior art describes the enormity of intermediary metabolites in view of structure comprising a lipid or a glycolipid; see Degroote et al., Sem in Cell & Dev Bio, 2004 and Sweeley, Pure & Appl. Chem., 1989. The prior art also describes a method of modulating an immune response in a mammalian subject comprising administering an effective amount of a specific mammalian intermediary metabolite which comprises a glycolipid, wherein the specific

intermediary metabolite is either a ganglioside or a glucocerebroside (see Gizurarson, US Patent 5942237).

Also discussed above is the enormity of differential structures of a glycosylceramide.

Working examples. The examples are drawn to the immunomodulatory effects of administering a *single* compound, glucocerebroside, wherein the effects include modulation of the number of NKT cells, CD4/CD8 ratio and glucose tolerance. The working examples fail to show how these immunomodulatory effects correlate to the actual treatment of any and all diseases derived from an inflammatory response or how this relates to mammalian intermediary metabolites of differential structures.

Guidance in the specification. The specification provides no guidance regarding how the administration of any and all mammalian intermediary metabolites may successfully treat any and all diseases derived from an inflammatory immune response. Further, there are no dosing regimens or time durations of treatment or structure to function correlation provided.

Predictability of the art. The ordinary artisan could not predict the correlation of an intermediary metabolite to its function in treating a broad genus of diseases. As noted above, the diseases listed in claim 157 are unrelated in origin, each of which may have distinct symptoms, etiologies, structures, nucleic acids, time course of incubation and infection, etc.

Amount of experimentation necessary. Based on the content of the instant specification, much undue experimentation would be necessary in order to determine if

treatment of an entire genus of diseases derived from an inflammatory immune response via administration of an entire genus of mammalian metabolites would be successful. The ordinary artisan would be required to generate actual data to determine if such successful treatment is possible. The specification fails to provide guidance on what structural characteristics of a glycosylceramide would be required, its required mechanism of action or its structure to function correlation to the instant claimed methods.

Given the discussion above, it would require undue experimentation for the ordinary artisan to perform the full scope of the method as claimed.

Response to Arguments

Applicant's arguments filed 1/3/2011 have been fully considered but they are not persuasive. Applicant notes that the claims are amended to read upon (in part) treatment with only beta-glycosylceramides and that one of ordinary skill in the art would "understand that the claimed methods would be effective with most if not all mammalian beta-glycosylceramides"; see p. 37 of Remarks.

This is not persuasive for at least the following reasons. First, it is noted that glycosylceramides includes a group of structurally, and thus, functionally, diverse compounds; see discussion above as well as the teachings by Sweeley. Separately, without any evidence provided by Applicant or any correlation between structure and function for the claim genus of compounds in the instant specification, it is unclear how this group of diverse compounds would be predicted "have generally similar biological activities" as asserted by Applicant.

Applicant submits that the examples show that treatment with beta-glycosylceramides reduces inflammatory immune responses and such a decrease would be expected to be an effective treatment for any disease where the pathogenensis of the disease is derived from an inflammatory immune response.

In response, it is noted here that is unclear from the instant specification if the administered glucocerebroside is indeed in its beta configuration. As discussed above, this limitation was not acknowledged at the time of filing. Separately, the claims are drawn to multiple *unrelated* diseases; see claim 157. Applicant has failed to provide any evidence that all of the diseases have a common inflammatory immune response or how modulation of any particular or a combination of responses would treat the unrelated diseases as claimed. Also see Adar and Ilan (2008) with respect to a glycosylceramide which provides that the same ligand can generate different types of immune responses in different immune microenvironments and may not result from the binding of a single ligand; see p. 216, col. 2. The authors further state that NKT lymphocytes are a heterogeneous population of cells that differ from one another in their CD1d reactivity and CD expression and changes in membrane properties may add to the variety of the responses; also see p. 216. Thus, the art teaches various immunomodulatory responses following administration of a beta-glycosylceramide would occur independent of the ligand itself due to a number of factors (e.g. membrane properties, microenvironments etc.), none of which was addressed in the instant specification; this supports a lack of predictability in the art.

Applicant further argues that the effectiveness of the treatment of any particular disease could be tested by routine experimentation without undue experimentation. Applicant further reiterates that "the skilled artisan would expect that any beta-glycosylceramide would likely be an effective treatment for any disease where the pathogenesis of the disease is derived from an inflammatory immune response…"; see p. 38 of Remarks.

Applicant is reminded that the claims are directed to a method of treatment of a disease and a method of inducing and characterizing the resulting immune responses are not equivalent to effective treatment. As noted in the previous action, the specification fails to provide any dosing regimens or time durations of treatment or structure to function correlations, leaving much undue experimentation to the skilled artisan to ascertain, if such is even possible. It is not clear how the characterized resulting immune responses would successfully achieve treatment of any disease wherein the pathogenesis is derived from an inflammatory immune response, given such was not adequately described.

Double Patenting-MAINTAINED

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-6 of copending Application No. 10/375, 906 (PGPUB 20040177522) in view of Stephenson and Zambon (*Occup. Med*, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite. Note that the claims of the '906 application are drawn to subjects with viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such diseases include viral influenza (see abstract of Stephenson and Zambon).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 50-52, 55-57, 59 and 60 of copending Application

No. 10/733,488 (PGPUB 20040171526) in view of Stephenson and Zambon (*Occup. Med*, 2002) and Hansen-Flaschen (*Ann Intern Med*, 2003). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite. Note that the claims of the '488 application are drawn to subjects with cancer, bacterial and viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such diseases include viral influenza (see abstract of Stephenson and Zambon), lung cancers and bacterial tuberculosis (see p. 322, col. 2 and p. 321, col. 1, respectively of Hansen-Flaschen).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 16, 17, 20, 22-24 and 64 of copending Application No. 10/733, 489 (PGPUB 20040171527) in view of Stephenson and Zambon (*Occup. Med*, 2002) and Hansen-Flaschen (*Ann Intern Med*, 2003). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite. Note that the claims of the '489 application are drawn to subjects with cancer and viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such

diseases include viral influenza (see abstract of Stephenson and Zambon) and lung cancers (see p. 322, col. 2 of Hansen-Flaschen).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 77-100 of copending Application No. 11/287,502 . Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 5 of copending Application No. 12/746, 430. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

In response to the double patenting rejections below, Applicant submits that a terminal disclaimer where necessary will be provide when a proper ODP resjection is the only rejection remaining in this application.

Until the rejections have been properly addressed, the rejections below are maintained for reasons of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is

(571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ZACHARIAH LUCAS can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Supervisory Patent Examiner, Art Unit 1648